

ACCELERATED ATHEROSCLEROSIS

- MAGNITUDE OF PROBLEM
- PHARMACOLOGICAL APPROACH
- MECHANISM: ROLE OF ENDOTHELIUM
- VASCULAR RECONSTRUCTION
- ENDOTHELIAL IMPLANTS

CARDIOVASCULAR DISEASES: ANNUAL STATISTICS

WORLD:

50,500,000 deaths

USA:

1,000,000 deaths

100,000,000 hospital days

1,500,000 procedures

40-50% failure rate

ACCELERATED ARTERIOPATHIES

PROCEDURE	TIME months	RESTENOSIS RATES
BALLOON ANGIOPLASTY	3	25-50%
LASER ANGIOPLASTY	6	35%
ATHERECTOMY	6	40-50%
ENDOVASCULAR STENTS	3	20-50%

MAGNITUDE OF PROBLEM

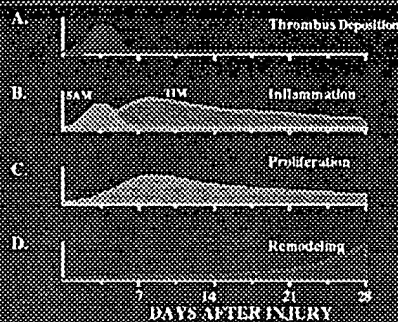
Angioplasty

Endovascular stents

Bypass grafts

Organ transplantation

FAILURE MODES



PHARMACOLOGICAL APPROACHES

HAVE FAILED

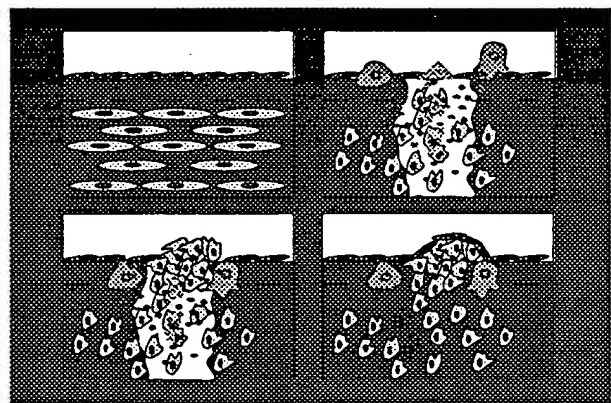
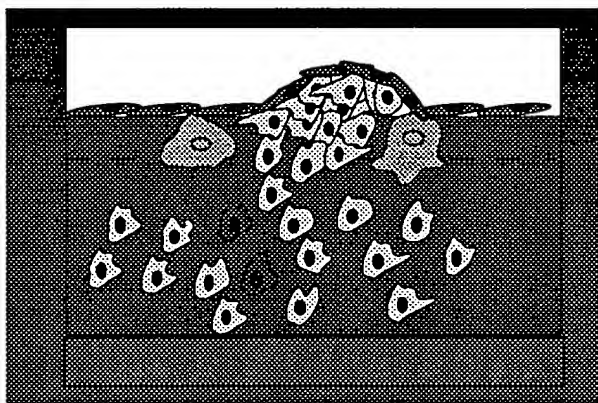
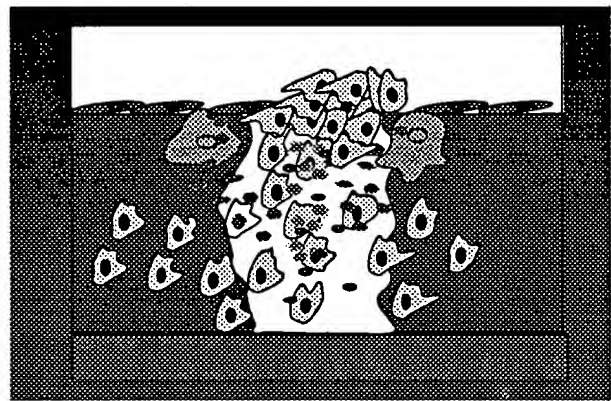
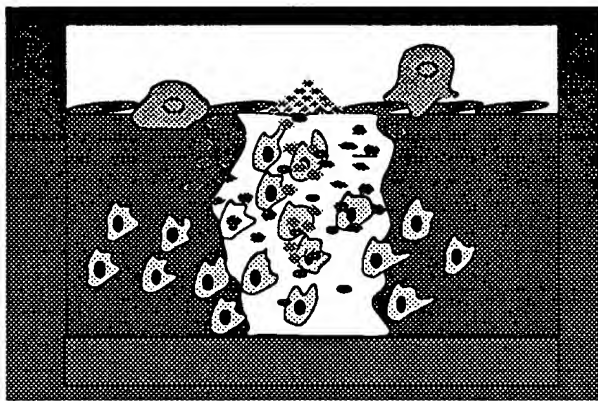
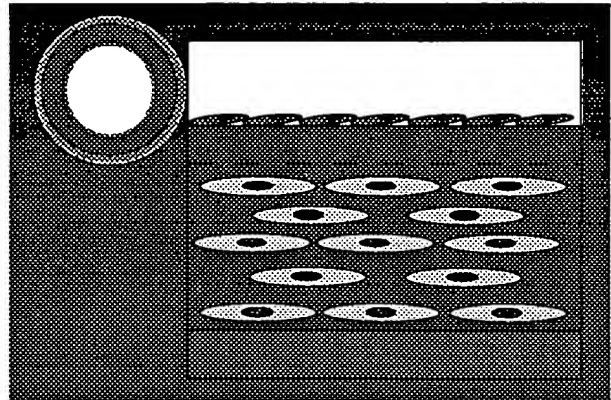
- multi-factorial mechanisms of accelerated atherosclerosis not handled by isolated drug administration
- drug therapy provides open loop, pharmacological dosing rather than physiological control

ACCELERATED ATHEROSCLEROSIS

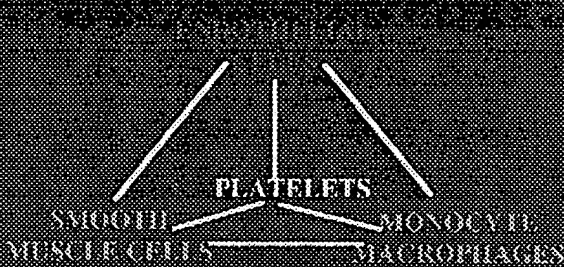
MECHANISM

ROLE OF ENDOTHELIUM

MODEL OF GROWTH CONTROL



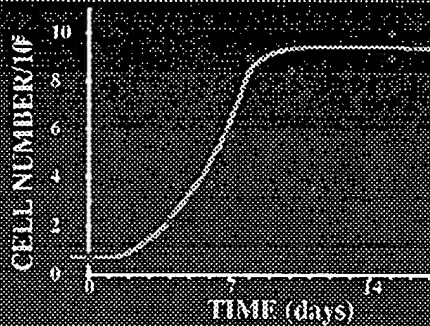
ENDOTHELIUM: CENTRALITY OF CELL BIOLOGY



VASCULAR RECONSTRUCTION

- Endothelial paving
- Endothelial transfection
- Complete arterial reconstruction
(Tissue engineering)

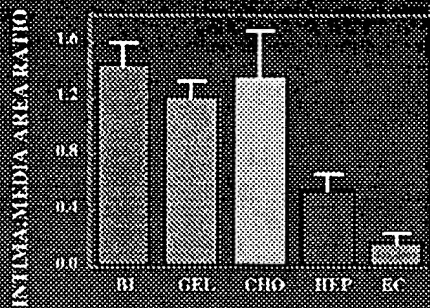
CELL GROWTH ON SCAFFOLD



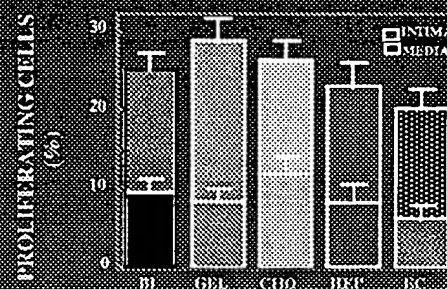
ENDOTHELIAL IMPLANTS

- implant placed outside of artery -
not at luminal interface
- not concerned with pharmacologic
levels of "drug" release

ENGRAFTS & INTIMAL HYPERPLASIA

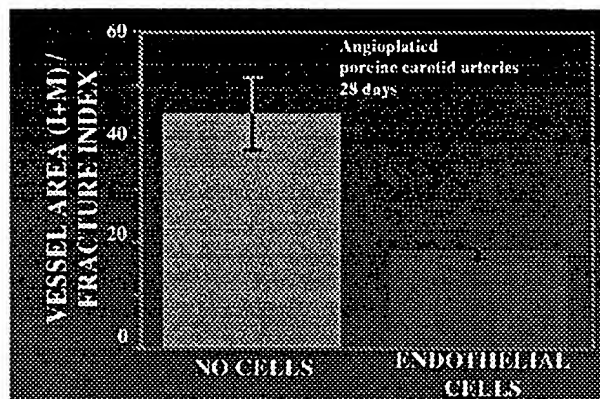
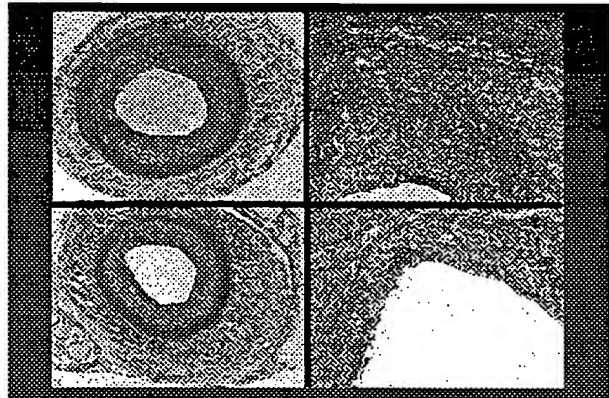


ENGRAFTS & CELL PROLIFERATION



MODELS OF DISEASE

rat	
carotid artery	heparin sensitive
balloon denudation	
porcine	
carotid artery	heparin insensitive
balloon overinflation	



ENDOTHELIAL IMPLANTS

- general impression that endothelium needed to be restored at luminal interface to exert effect
- endothelial restoration inefficient and transient
- there is normal endothelium adjacent to denuded or injured endothelium and it cannot control disease
- models and disease that are resistant to the infusion of endothelial products

ENDOTHELIAL IMPLANTS

- recapitulate biochemical control without reconstructing the arterial architecture
- significant departure from controlled drug delivery
- physiological control without pharmacological dosing



Creation date: 05-05-2005
Indexing Officer: LCHEO - LEE CHEO
Team: OIPEBackFileIndexing
Dossier: 08458978

Legal Date: 10-21-1997

No.	Doccode	Number of pages
1	EXIN	5
2	IDS	6

Total number of pages: 11

Remarks:

Order of re-scan issued on